In the Claims:

This listing of claims will replace all prior versions and listings of the claims in this application.

Listing of Claims

1. (Currently Amended) A method of introducing at least one functional exogenous human cytochrome P450 into a non-human cell ~~cell(s) whose own~~ having inactive endogenous cytochrome P450s ~~have been rendered inactive~~, the method comprising introducing DNA encoding said at least one exogenous human cytochrome P450 ~~such that said~~ to provide at least one functional human cytochrome P450 whereas the ~~remains functional where the cell's own~~ endogenous cytochrome P450s are inactive.

2. (Currently Amended) The [[A]] method according to claim 1 wherein an endogenous cytochrome P450 reductase (CPR) gene is deleted from the genome of the non-human cell ~~the non-human cell's own endogenous P450s are rendered inactive by deletion of the endogenous CPR gene~~ and ~~where~~ wherein the function of the at least one ~~introduced~~ exogenous human cytochrome P450 is maintained ~~either~~ by modifying the exogenous human cytochrome P450 to ~~it being in modified form such that it can~~ function independently of ~~any~~ a separate CPR ~~protein~~ moiety or ~~by~~ introducing into the non-human cell a DNA encoding a CPR gene to provide an exogenous CPR moiety to interact with the exogenous human cytochrome P450 ~~such that said at least one introduced human P450 can function in the non-human animal cell(s)~~.

3. (Currently Amended) The [[A]] method according to ~~either preceding~~ claim 1 wherein the non-human ~~cell(s) is/are~~ cell is derived from a monkey, dog, cat, rabbit, hamster, rat, or mouse.

4 (Currently Amended) The [[A]] method according to claim 3 wherein the non-human ~~cell(s) is/are~~ cell is derived from a mouse.

5. (Currently Amended) The [[A]] method according to ~~any preceding~~ claim 1 wherein a plurality of DNA sequences encoding different human cytochrome P540s are introduced into the non-human ~~cell(s)~~ cell.

6. (Currently Amended) The [[A]] method according to ~~any preceding~~ claim 1 wherein the human cytochrome P450 is selected from the group comprising 3A4, 2D6, 2C9, 1A2, 2C19 and 2C8.

7. (Currently Amended) The [[A]] method according to ~~any preceding~~ claim 1 wherein enzymatically active human cytochrome P450 enzymes are expressed through expression of ~~expression of the human cytochrome P450 as either, part of~~ a fusion protein comprising a cytochrome P450 moiety [[-]] and a cytochrome P450 reductase ~~fusion~~ protein or co-expression of ~~the~~ a separate human cytochrome P450 moiety and ~~with~~ a separate cytochrome P450 reductase protein~~, results in enzymatically active human P450 enzymes~~.

8. (Currently Amended) The [[A]] method according to ~~any preceding~~ claim 7 wherein expression of the human cytochrome P450 ~~as either, part of a cytochrome P450 cytochrome P450 reductase fusion protein or co-expression of the human cytochrome P450 with a separate cytochrome P450 reductase are~~ is driven by a gene promoter.

9. (Currently Amended) The [[A]] method according to claim 8 [[7]] wherein the promoter is CMV_2 [[or]] a tissue-specific rat albumin promoter or CYP1A1.

10. (Currently Amended) The [[A]] method according to ~~any one of claims 6 to 9~~ claim 7 wherein expression of the fusion protein or co-expression of the separate human cytochrome P450 moiety and the P450 reductase protein ~~fusion proteins is/are~~ is constitutive or conditional.

11. (Currently Amended) The [[A]] method according to ~~any of claims 6 to 10~~ claim 7 wherein the fusion protein or co-expression of the separate human cytochrome P450 moiety and the P450 reductase protein ~~fusion proteins is/are~~ is targeted to a specific cellular component where non-human animal P540s are not expressed.

12. (Currently Amended) The [[A]] method according to ~~any preceding~~ claim 11 wherein an intracellular targeting sequence is added to the fusion protein or co-expressed with the separate human cytochrome P450 moiety and the P450 reductase protein ~~fusion proteins~~.

13. (Currently Amended) The [[A]] method according to ~~any preceeding~~ claim 1 further including the step of introducing into a non-human cell at least one ~~further~~ DNA sequence encoding a human ~~protein/enzyme~~ protein involved in xenobiotic metabolism other than a cytochrome P450 ~~that is involved in xenobiotic metabolism~~.

14. (Currently Amended) The [[A]] method according to claim 13 wherein the at least one ~~further~~ DNA sequence encoding [[a]] the human protein encodes a drug transporter protein.

15. (Currently Amended) The [[A]] method according to claim 14 wherein the DNA sequence encoding [[a]] the human protein encodes Mdr.

16. (Currently Amended) A method of assessing human cytochrome P450-mediated metabolism, comprising using ~~Use of~~ a transgenic animal, tissues and/or or cells ~~produced by the method according to any preceding claim that have been modified to contain and express~~ comprising a DNA encoding at least one human P450 and/or another protein involved in metabolism ~~so as to investigate human P450 mediated metabolism in said a transgenic animal, tissues and/or cells derived therefrom~~.

17. (Currently Amended) [[Use]] The method according to claim 16 wherein results of the assessment of human cytochrome P450-mediated metabolism correlates to assessment of ~~in investigation~~ disease states selected from the group ~~comprising~~ consisting of choleastasis, artherogenesis, hormonal imbalances, neurological disorders, degenerative diseases, skin conditions, cardiovascular disease, cancer and glaucoma and any other disease in which P450s play a role.

18. (Currently Amended) ~~Use~~ A method of using human cells introduced into an immune-deprived reductase null animal ~~so as~~ to investigate contribution of said human cells in P450-mediated product metabolism and/or toxicity and/or drug candidate screening.

19. (Currently Amended) [[A]] The method according to claim 18 wherein said human cells are hepatocytes.

20. (Original) A CYP3A4/CPR transgenic HRN™ mouse.

21. (Original) Use of a mouse according to claim 20 in pre-clinical and toxicity studies.